

REMARKS

Claims 11, 17, and 54-64 are currently pending. Claims 11 and 17 are amended. The amendments find support in the specification and claims as originally filed and do not add new matter. Specific support for the amended claims is discussed in further detail below.

At the outset, Applicants would like to thank Examiner Steele for taking time to discuss the rejections set out in the Office Action with Applicants' representative on September 5, 2007. During the telephone interview, the rejections under §112, second paragraph and §102 were discussed. The substance of the interview is incorporated into Applicants' remarks below.

Formal Matters

Specification

The Office Action states that the specification is objected to because a literature citation on page 55 did not include the volume number of the cited journal. Applicants have amended the specification to correct this typographical error and request that the objection be reconsidered and withdrawn.

Rejection of Claims 11, 17, and 54-64 Under 35 U.S.C. §112, Second paragraph

"Continuous lines"

The Office action states that claims 11, 17, and 54-64 are rejected under §112, second paragraph for alleged indefiniteness in the recitation of a "continuous line(s)." The Office Action states that while the specification defines a line as having the dimensions of a line, the specification also teaches that the line could be made of a series of droplets that "'coalesce' into a 'circle'" (Office Action, page 4). During the telephone interview on September 5, 2007, the Examiner indicated that the term "continuous line" is clear on its face, but the definitions in the specification make the

term unclear. Specifically, the Examiner stated that the definition of the terms "continuous" and "line" would encompass a spot, a meaning that would be deemed by one of skill in the art to be repugnant to the plain and ordinary meaning of a continuous line. Applicants respectfully disagree and traverse the rejection.

The specification defines the term "line" to mean a "continuous distribution of an individual member of a repertoire having the physical shape of a line. (Specification, p. 26). The specification states that a line preferably has dimensions such as "XX long and YY wide." Id. The specification defines "continuous" as referring to the fact that "an individual member of a repertoire on an array is present along the entire length of the line." (Specification, p. 30-31). There is no teaching in the specification that renders ambiguous either the plain and ordinary meaning of "continuous line" or the meaning provided by the definitions in the specification.

The language cited in the Office Action, however, relating to teachings in the specification that the line can be " 'a series of droplets' that 'coalesce' into a 'circle' [which] could be a spot" (Office Action page 4) is taken out of context to support the rejection. The specification teaches that the lines of the invention can be disposed in various configurations including "straight parallel lines, disposed at an angle to straight parallel lines; concentric circles or polygons, used together with a star of radial lines" (Specification, page 4). The specification teaches that a line "may refer to a series of droplets which are placed on a solid surface, and which coalesce **to form a continuous line** of solution" (Specification, page 26, emphasis added). The specification, in contrast to the assertion in the Office Action, does not teach that a line can be a series of droplets that coalesce to form a circle which is a spot. Indeed, the specification explicitly states that, in the context of a series of drops coalescing, they can coalesce **to form a continuous line**. This is entirely contrary to the assertion in the Office Action that the term "continuous line" would encompass a spot. Moreover, there is no reasonable interpretation of the claims or specification that would lead one of skill in the art to question whether Applicants were attempting to encompass the ambiguous meaning of "continuous line" advanced in the Office Action. The claims clearly state a "continuous line;" there is no reasonable interpretation of the claims

when read in view of the specification that would create ambiguity as to whether a "continuous line" is describing a "spot."

The Office Action states that the dimensions of XX long and YY wide would not be readily ascertained by one of skill in the art. Applicants disagree. The inclusion of the XX and YY dimensions in the definition of a "line" was merely to clarify that a line can be defined in terms of length and width; this is in contrast to a circular spot, which would be defined in terms of diameter, radius, or perimeter. One of skill in the art would be clearly apprised of whether they were practicing the invention using a line and neither the claims nor the definition of a line require one of skill in the art to make a measurement of the length or width of the line, although such a measurement would be well within the ordinary skill in the art.

It is well settled law that §112, second paragraph assures that the claims in a patent are sufficiently precise to permit a potential competitor to determine whether or not they are infringing. See, e.g., *Amgen Inc. v. Hoescht Marion Roussel, Inc.*, 314 F.3d 1313 (Fed. Cir. 2003). Again, Examiner Steele stated in telephone interview of September 5, 2007 that the term "continuous line" is clear and unambiguous, but that the definition in the specification creates ambiguity. As noted above, the definitions in the specification clearly and unambiguously define the metes and bounds of a "continuous line." One of skill in the art, reading the claims in view of the specification, would be able to clearly determine whether or not they fall under the claims. Accordingly, Applicants request that the rejection be reconsidered and withdrawn. To the extent that the Examiner maintains the rejection, Applicants respectfully request that the Examiner point out the entire passages or sentences in the specification that the Examiner believes create ambiguity or uncertainty in the meaning of "continuous line."

"Juxtaposed"

The Office Action states that claims 11, 17, and 54-64 are rejected under §112, second paragraph as indefinite in the recitation of "juxtaposed." The Office Action states that the term is not defined by the claims and one of skill in the art would not be reasonably apprised of the scope of the invention. The Office Action provides

examples of arrangements of lines that could fall under the meaning of "juxtaposed" that would render the claim indefinite (e.g., two microfuge tubes placed within 20 μ m of each other). Applicants respectfully disagree and traverse the rejection.

The specification clearly defines the term "juxtaposed" as an arrangement of two or more repertoires such that the molecules in the repertoires are capable of interacting with one another. Specification, page 29. Without acquiescing to the rejection and solely for the purpose of further clarifying the claimed subject matter, Applicants have amended claims 11 and 17 to include the limitation that the members of the repertoires are juxtaposed "such that members of the first and second repertoire are able to interact." Support for this amendment is found in the specification at page 29, lines 15-17. This amendment should obviate the concern voiced in the Office Action that the term "juxtaposed" could encompass "a microcentrifuge tube placed within 20 μ m of another tube...a streaked plate with colonies along the streak, a lane in a gel within 20 μ m of another lane." In addition, the Office Action also states that juxtaposed repertoires could include "a line (e.g., spot) dropped on top of another spot." This is clearly not encompassed by the claims, since, as described above, a spot is not a continuous line.

Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Rejection of Claims 11, 17, and 64 Under 35 U.S.C. §102(b)

The Office Action states that claims 11, 17, and 64 are rejected under §102(b) as anticipated by Bussow et al. The Office Action states that Bussow et al. teach gridding cells onto filter membranes and "adding a 'stream'" of monoclonal antibody thus creating two- or three-chain polypeptides. Applicants disagree and traverse the rejection.

It is well settled law that to anticipate a claim, a prior art reference must teach, either expressly or inherently, each element of the claimed invention. See, e.g., *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005).

Applicants have reviewed the entire teachings of Bussow et al. and can find no teaching of a method for generating a two- (or three-) chain polypeptide comprising providing an array comprising a solid surface that includes said first repertoire of single chain polypeptides deposited on the solid surface in a first series of continuous lines that do not intersect with each other, and said second repertoire of single chain polypeptides deposited on the solid surface in a second series of continuous lines that do not intersect with each other (and a third repertoire deposited in a third series of continuous lines), wherein each line of the first series of lines intersects with each line of the second series of lines (and the third series of lines) such that each member of the first repertoire is juxtaposed with each member of the second repertoire (and each member of the third repertoire) such that members of the first repertoire are able to interact with members of the second repertoire (and third repertoire), thereby generating two- (or three-) chain polypeptides at the intersection of said first and second (and third) series of lines, thereby creating a combinatorial library of two- (or three-) chain polypeptides.

Bussow et al. does not teach or even suggest depositing a first or second (or third) repertoire of molecules on a solid surface in a series of continuous lines. The teachings of Bussow et al. are limited to gridding of bacterial colonies on a surface. The figure legend for Figure 1 states that gridding patterns of 3x3 or 5x5 were used; that is a pattern of 3x3 spots or 5x5 spots. Thus, when referring to "gridding" Bussow et al. is referring to spotting onto a surface, not depositing bacterial colonies (or anything else) in a series of continuous lines. Moreover, even if the bacterial colonies were to be considered analogous to the first repertoire recited in the instant claims, there is not teaching in Bussow et al. of depositing a second repertoire of molecules on the surface in a second series of continuous lines such that the lines of the first series intersect with the lines of the second series.

Accordingly, Bussow et al. does not teach each element of the instantly claimed invention and, therefore, does not anticipate. Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Rejection of Claims 11, 17, 54-56, 59-61, and 64 Under 35 U.S.C. §102(b)

The Office Action states that claims 11, 17, 54-56, 59-61, and 64 are rejected under §102(b) as allegedly anticipated by Rowe et al. The Office action states that Rowe et al. teach "methods for producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical channels comprise antibodies and adding samples flowed through horizontal channels...therein the vertical and horizontal channels are at 90° angles." The Office Action concludes that these teachings anticipate the claimed invention. Applicants respectfully disagree and traverse the rejection.

As noted above, in order to anticipate the claimed invention, a prior art reference must teach, either expressly or inherently, each element of the claimed invention. See, e.g., *Perricone v. Medicis Pharmaceutical Corp.*, 432 F.3d 1368 (Fed. Cir. 2005).

Rowe et al. does not teach or suggest the claimed method comprising a solid surface on which a first and second (and third) repertoire are "deposited" in a "series of continuous lines." During the telephone interview of September 5, 2007, Applicants pointed out to the Examiner that Rowe et al. teaches patterning of capture antibodies in vertical "stripes" on a surface, Rowe et al. does not teach a second repertoire present on the solid surface in a series of continuous lines. Rowe et al. teaches that analyte is "flowed" through horizontally oriented channels which are then "rinsed," such that the only place on the solid surface that the analyte is present in where it has been bound by a capture antibody; that is, the analyte is not "present" on the surface in a series of continuous lines, it is only present on the surface at the point where it is bound by the capture antibody (See Figure 2A of Rowe et al.). To further clarify this point, Applicants have amended claims 11 and 17 to recite that the first and second repertoires are "deposited" in a first and second series of continuous lines. The specification defines the term "deposited" on page 31, stating that depositing refers "to the step of placing a member of a repertoire of the present invention on a solid surface, such that the member becomes stably associated with the surface." The specification defines "stably

associated” as referring to “a repertoire member that is bound to the solid substrate to form an array via covalent bonds, hydrogen bounds or ionic interactions...such that the repertoire member retains its unique pre-selected position...under conditions in which an array is typically analyzed (i.e., during one or more steps of hybridization, washes, and/or scanning, and the like).” Thus the claims, as amended, require placing a repertoire on the solid surface in a series of continuous lines such that the member becomes stably associate with the surface. As noted above, Rowe et al. do not teach placing the analyte (analogous to the second repertoire) in a series of continuous lines that become stably associated with the surface; in fact, the analyte flowed through the horizontal channels does not become stably associate with the surface in a series of continuous lines. Rowe et al. teaches washing unbound analyte from the flow channels, thus, evidencing the fact that the analyte is not stably associated with the solid surface in a series of continuous lines since the repertoire members do not retain their position under wash conditions (see definition of “stably associated” above). The only place the analyte of Rowe et al. associates with the surface is at the point where the analyte contacts the correct antibody. Thus, Rowe et al. does not teach a solid surface in which members of a first and second repertoire are deposited in a first and second series of continuous lines.

Accordingly, Rowe et al. does not teach each element of the claimed invention and Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Rejection of Claims 11, 17, and 54-64 under 35 U.S.C. §103(a)

The Office Action states that claims 11, 17 and 54-64 are rejected under §103 as unpatentable over the teachings of Rowe et al. in view of Stevens et al. The Office Action applies Rowe et al. as described above, but notes that Rowe et al. does not teach making Vh-Vh or VI-VI two-chain polypeptides or two-chain polypeptides bound to antigen to generate a three-chain polypeptide. The Office Action states that Stevens et al. teaches methods of making recombinant antibody subunit dimers and screening against antigen, and concludes that it would have been obvious to modify the

method of producing two- or three-chain polypeptides as allegedly taught by Rowe et al. to include the Vh-Vh and VI-VI dimers taught by Stevens et al. Applicants disagree and traverse the rejection.

It is well established that to render a claim obvious, the prior art reference (or references when combined) must teach or suggest all the claim limitations. In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974).

As stated above, Rowe et al. does not teach each element of the invention recited in independent claims 11 and 17 (nor does Rowe et al. teach each element of the invention recited in dependent claims 54-64). There is no teaching in Stevens et al. that supplements the deficient teachings in Rowe et al. to arrive at the claimed invention. Thus, even if the teachings of Rowe et al. and Stevens et al. are considered together, the resulting combination does not teach a method of generating a two- or three-chain polypeptide by depositing a first and second, and optionally third series of continuous lines on a surface such that the lines of each series intersect with the lines of the other series, such that each member of each repertoire is juxtaposed with each other member of each other repertoire. Accordingly, the combination cited in the Office Action does not teach each limitation of the amended claims, and does not render the instant claims *prima facie* obvious.

Applicants, therefore, request that the rejection be reconsidered and withdrawn.

Obviousness-type Double Patenting

The Office Action states that the instant claims are rejected as unpatentable under the doctrine of obviousness-type double patenting in view of applications 11/413,427 and 09/888,313. Upon notification of otherwise allowable subject matter in this instant application, Applicants will consider the allowed claims in view of the cited applications and file a terminal disclaimer where appropriate.

The Office Action also states that claims 11, 17, and 54-64 are rejected under the doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of copending application 10/161,145. In order to reach a finding of obviousness-type double patenting, the invention defined in the instant claims must be anticipated by or an obvious variation of the invention defined in the cited application. See, MPEP §804(B)(1)(a). The claims of the instant application would not be obvious in view of the claims in copending application 10/161,145 ("the '145 application"). The claims of the '145 application relate to screening molecules for interactions with target molecules and includes steps of arraying nucleic acids on a solid support and expressing the nucleic acids on the solid support. There is no teaching in the claims of the '145 application to suggest to one of skill in the art to deposit a first and second repertoire on a solid surface in a first and second series of continuous lines, such that all lines of the first series intersect with all lines of the second series such that each molecule in the first repertoire is juxtaposed to each molecule in the second repertoire such that they are able to interact. In addition, the claims of the instant invention relate to the generation of a combinatorial library of two- or three-chain **polypeptides**. The claims of the '145 application relate to detecting interactions between a polypeptide and a target molecule; the target molecules can include small molecules and metal ions (claim 15). Thus, not only would it be non-obvious for one of skill in the art to arrange the nucleic acids and target molecules of the '145 claims in the specific arrangement of the instant invention, but it would also not be obvious, based on the '145 claims, to generate a combinatorial library of two- or three-chain polypeptides. The Office Action has not provided any rationale to support its contention that the instant claims would be obvious in view of the claims of the '145 patent. Similarly, the Office Action has not provided any rationale to support the contention (inherent in a double patenting rejection) that the granting of the instant claims would result in an unjustified timewise extension of the rights granted by any patent issued from the '145 application.

Accordingly, Applicants request that the rejection with respect to the '145 application be reconsidered and withdrawn.

The Office Action also states that the instant claims are rejected under the doctrine of obviousness-type double patenting in view of the claims of U.S. application 10/161,144. Applicants disagree and traverse the rejection.

The claims of the instant application would not be obvious in view of the claims of the 10/161,144 application ("the '144 application"). The claims of the '144 application relate to methods for isolating from a naïve immunoglobulin superfamily repertoire, a polypeptide that interacts with a specific target ligand. There is no teaching in the '144 claims that would suggest to one of skill in the art to deposit a first and second repertoire on a solid surface in a first and second series of continuous lines, such that all lines of the first series intersect with all lines of the second series such that each molecule in the first repertoire is juxtaposed to each molecule in the second repertoire such that they are able to interact so as to generate a combinatorial library of two- or three-chain polypeptides. Moreover, the claims of the '144 application are focused on isolating polypeptides from a naïve immunoglobulin superfamily repertoire, and would not render obvious a method of generating two- or three-chain polypeptides. The Office Action has not provided any support as to why one of skill in the art, given the '144 claims, would be motivated to practice a method of generating a library of two- or three-chain polypeptides according to the specific limitations recited in the instant claims, or why the instant claims are an obvious variation of the method recited in the '144 application claims. In addition, the Office Action has not provided any rationale to support the contention (inherent in a double patenting rejection) that the granting of the instant claims would result in an unjustified timewise extension of the rights granted by any patent issued from the '144 application.

Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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